UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,439	10/24/2001	Andrew Saxon	UC067.004A	9201

77845 7590 09/23/2008

Goodwin Procter LLP
Attn: Patent Administrator
135 Commonwealth Drive
Menlo Park, CA 94025-1105

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
09/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/000,439	SAXON, ANDREW	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,21 and 69-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,21,70 and 72* is/are rejected.

7)☒ Claim(s) *69 and 71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 30, 2008 has been entered.

2. Claims 17, 21 and 69-72 are pending are being acted upon in this Office Action.

3. In view of the claims amendment filed June 30, 2008, the new matter rejection of claims 17, 21-24, 26-34, 40-44 and 60-68 under 35 U.S.C. 112, first paragraph has been obviated.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 17, 21, 70 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an isolated fusion molecule as set forth in claims 69 and 71 for treating anaphylactic response which may result from exposure to exogenous myelin basic protein polypeptide as would be encountered during tolerance therapy, **does not** reasonably provide enablement for any isolated fusion molecule comprising a first polypeptide sequence comprising a native human IgG heavy chain constant region capable of specific binding to a native human IgG inhibitory receptor, wherein said native human IgG heavy chain constant region sequence is the native human IgG heavy chain constant region sequence of SEQ ID NO: 2 or SEQ ID NO: 3 directly functionally connected to a second polypeptide sequence consisting of minimal MBP epitope *having* the sequence of SEQ ID NO: 13 as set forth in claims 17, 21, 70 and 72. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Enablement is not commensurate in scope with how to make and use such fusion proteins mentioned above wherein the second polypeptide consisting of minimal MBP having the sequence of SEQ ID NO: 13 for treating multiple sclerosis.

The specification discloses only an isolated fusion molecule comprising a first polypeptide consisting of the amino acid sequence of a hinge-CH2-CH3 of human IgG1 constant region of SEQ ID NO: 2 or the amino acid sequence of SEQ ID NO: 3 fused to a myelin basic protein T epitope *consisting of* the amino acid sequence of SEQ ID NO: 13, see page, 80, Example 2 or the full-length sequence for treating anaphylactic response which may result from exposure to exogenous myelin basic protein polypeptide as would be encountered during tolerance therapy.

The term "having" is open-ended. It expands the minimal MBP epitope consisting of the amino acid sequence of SEQ ID NO: 13 to include additional amino acids at either or both ends. There is a lack of guidance as to which amino acids to be added to the MBP epitope such that the resulting fusion protein still generated antibody specific to the MBP epitope and binds to FcγRIIb.

Skolnick *et al*, of record; PTO 1449, teach that squence-based methods for function prediction are inadequate and knowing a protein's structure does not necessary tell one it's function (See entire document, Abstract in particular).

Warren et al (of record, abstract) teach administering myelin basic protein fragment such as MBP35-58 to multiple sclerosis patient had no effect on the anti-MBP level. However, only administering MBP 75-95 resulted in a significant in the autoantibodies over a period of one month (see abstract, in particular).

Vanderlugt et al (of record, J immunology 164: 670-678, 2000; PTO 892) teach the mechanism(s) underlying the initiation and progression of autoimmune disease are not well understood. A number of recent studies in both animal models of autoimmune disease and their

human counterparts have shown that administering autoantigen causes epitope spreading, i.e., the de novo activation of autoreactive T cells by autoepitopes released secondary to inflammatory tissue damage (see page 670, col. 1, in particular). Vanderlugt et al teach clinical relapses are associated with the development of T cell response to newly emerging epitopes on the same PLP (i.e., intramolecular epitope spreading to distinct epitope) and/or different myelin epitopes (i.e., intermolecular epitope spreading to MBP epitopes), se page 676, col. 2, in particular. The process of epitope spreading has obvious important implications for the design of antigen-specific therapies for the treatment of autoimmune disease such as multiple sclerosis since these therapies will have to identify and target endogenous self epitopes associated with chronic tissue destruction. Peptide specific therapy will have to be individualized for every patient due to the myriad of potential organ-specific autoepitopes and extensive MHC diversity (see page 677, col. 2, in particular). Vanderlugt et al conclude that because determining the specificity and hierarchical order of autoantigen epitope spreading in human disease such as multiple sclerosis is not currently feasible, antigen-specific therapies for ongoing treatment autoimmune disease may require additional treatment such as induction of tolerance using whole tissue extracts, mixtures of encephalitogenic proteins/peptides or costimulatory blockade (see page 677, col. 2, in particular).

Blanas et al (of record, Science 274: 1707-1709, Dec 1996; PTO 1449) teach treating autoimmune rheumatoid arthritis and multiple sclerosis by oral administering autoantigen could lead to onset of autoimmune diabetes (see abstract, in particular).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed June 30, 2008 have been fully considered but are not found persuasive.

Applicant's position is that claims have been amended to conforms to the content suggested by the Examiner in the Office Action mailed 4/1/2008, page 2, section 5, lat paragraph; page 3, section 6, first paragraph; page 5, first paragraph and page 6, last paragraph.

Contrary to applicants' assertion that the claims have been amended to conforms to the content suggested by the Examiner in the Office Action, the amended claims 17, 21, , 70 and 72 still recite an isolated fusion protein ...the second polypeptide ...*having* the sequence of SEQ ID NO: 13.

The term "having" is open-ended. It expands the minimal MBP epitope consisting of the amino acid sequence of SEQ ID NO: 13 to include additional amino acids at either or both ends. There is a lack of guidance as to which amino acids to be added to the MBP epitope such that the resulting fusion protein still generated antibody specific to the MBP epitope and binds to FcγRIIb.

Skolnick *et al*, of record; PTO 1449, teach that squence-based methods for function prediction are inadequate and knowing a protein's structure does not necessary tell one it's function (See entire document, Abstract in particular).

Warren et al (of record, abstract) teach administering myelin basic protein fragment such as MBP35-58 to multiple sclerosis patient had no effect on the anti-MBP level. However, only administering MBP 75-95 resulted in a significant in the autoantibodies over a period of one month (see abstract, in particular).

Vanderlugt et al (of record, J immunology 164: 670-678, 2000; PTO 892) teach the mechanism(s) underlying the initiation and progression of autoimmune disease are not well understood. A number of recent studies in both animal models of autoimmune disease and their human counterparts have shown that administering autoantigen causes epitope spreading, i.e., the de novo activation of autoreactive T cells by autoepitopes released secondary to inflammatory tissue damage (see page 670, col. 1, in particular). Vanderlugt et al teach clinical relapses are associated with the development of T cell response to newly emerging epitopes on the same PLP (i.e., intramolecular epitope spreading to distinct epitope) and/or different myelin epitopes (i.e., intermolecular epitope spreading to MBP epitopes), se page 676, col. 2, in particular. The process of epitope spreading has obvious important implications for the design of antigen-specific therapies for the treatment of autoimmune disease such as multiple sclerosis since these therapies will have to identify and target endogenous self epitopes associated with chronic tissue destruction. Peptide specific therapy will have to be individualized for every patient due to the

myriad of potential organ-specific autoepitopes and extensive MHC diversity (see page 677, col. 2, in particular). Vanderlugt et al conclude that because determining the specificity and hierarchical order of autoantigen epitope spreading in human disease such as multiple sclerosis is not currently feasible, antigen-specific therapies for ongoing treatment autoimmune disease may require additional treatment such as induction of tolerance using whole tissue extracts, mixtures of encephalitogenic proteins/peptides or costimulatory blockade (see page 677, col. 2, in particular).

Blanas et al (of record, Science 274: 1707-1709, Dec 1996; PTO 1449) teach treating autoimmune rheumatoid arthritis and multiple sclerosis by oral administering autoantigen could lead to onset of autoimmune diabetes (see abstract, in particular).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

6. Claims 17, 21, 70 and 72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing nucleotide sequences, and biological functions. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., complete or partial structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, method of making the claimed invention, level of skill and knowledge in the art and predictability in the art sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for any isolated fusion molecule comprising a first polypeptide sequence comprising a native human IgG heavy chain constant region capable of specific binding to a native human IgG inhibitory receptor, wherein said native human IgG heavy chain constant region sequence is the native human IgG heavy chain constant region sequence of SEQ ID NO: 2 or SEQ ID NO: 3 directly functionally connected to a second polypeptide sequence consisting of minimal MBP epitope *having* the sequence of SEQ ID NO: 13 as set forth in claims 17, 21, 70 and 72.

At the time of filing, the specification discloses only an isolated fusion molecule comprising a first polypeptide consisting of the amino acid sequence of a hinge-CH2-CH3 of human IgG1 constant region of SEQ ID NO: 2 or the amino acid sequence of SEQ ID NO: 3 fused to a myelin basic protein T epitope *consisting of* the amino acid sequence of SEQ ID NO: 13, see page, 80, Example 2 or the full-length sequence for treating anaphylactic response which may result from exposure to exogenous myelin basic protein polypeptide as would be encountered during tolerance therapy.

Other than the full-length myelin basic protein comprising the amino acid sequence of SEQ ID NO: 12 or the specific myelin basic protein epitope consisting of the amino acid sequence of SEQ ID NO: 13 directly functionally fused to a native human IgG heavy constant region sequence of SEQ ID NO: 2 or SEQ ID NO: 3, the specification does not describe other members of the myelin basic protein epitope longer than the sequence of SEQ ID NO: 13 by structure.

The term "having" is open-ended. It expands the minimal MBP epitope consisting of the amino acid sequence of SEQ ID NO: 13 to include additional amino acids at either or both ends.

There is a lack of guidance as to which amino acids to be added to the MBP epitope such that the resulting fusion protein still generated antibody specific to the MBP epitope and binds to FcγRIIb.

Skolnick *et al*, of record; PTO 1449, teach that squence-based methods for function prediction are inadequate and knowing a protein's structure does not necessary tell one it's function (See entire document, Abstract in particular).

Warren et al (of record, abstract) teach administering myelin basic protein fragment such as MBP35-58 to multiple sclerosis patient had no effect on the anti-MBP level. However, only administering MBP 75-95 resulted in a significant in the autoantibodies over a period of one month (see abstract, in particular).

Because the described one species of minimal MBP epitope is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, one of skill in the art would conclude that applicant was not in procession of the claimed genus to show that the applicant would have been in possession of the claimed genus as a whole at the time of filing for the claimed fusion protein. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 17, 21, 70 and 72.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115). Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

Applicants' arguments filed June 30, 2008 have been fully considered but are not found persuasive.

Applicant's position is that claims have been amended to conforms to the content suggested by the Examiner in the Office Action mailed 4/1/2008, page 2, section 5, lat paragraph; page 3, section 6, first paragraph; page 5, first paragraph and page 6, last paragraph.

Contrary to applicants' assertion that the claims have been amended to conforms to the content suggested by the Examiner in the Office Action, the amended claims 17, 21, , 70 and 72

still recite an isolated fusion protein ...the second polypeptide ...*having* the sequence of SEQ ID NO: 13.

The term "having" is open-ended. It expands the minimal MBP epitope consisting of the amino acid sequence of SEQ ID NO: 13 to include additional amino acids at either or both ends. There is a lack of guidance as to which amino acids to be added to the MBP epitope such that the resulting fusion protein still generated antibody specific to the MBP epitope and binds to FcγRIIb.

Skolnick *et al*, of record; PTO 1449, teach that squence-based methods for function prediction are inadequate and knowing a protein's structure does not necessary tell one it's function (See entire document, Abstract in particular).

Warren et al (of record, abstract) teach administering myelin basic protein fragment such as MBP35-58 to multiple sclerosis patient had no effect on the anti-MBP level. However, only administering MBP 75-95 resulted in a significant in the autoantibodies over a period of one month (see abstract, in particular).

At the time of filing, the specification discloses only an isolated fusion molecule comprising a first polypeptide consisting of the amino acid sequence of a hinge-CH2-CH3 of human IgG1 constant region of SEQ ID NO: 2 or the amino acid sequence of SEQ ID NO: 3 fused to a myelin basic protein T epitope *consisting of* the amino acid sequence of SEQ ID NO: 13, see page, 80, Example 2 or the full-length sequence for treating anaphylactic response which may result from exposure to exogenous myelin basic protein polypeptide as would be encountered during tolerance therapy.

As of the filing of instant application, applicants are not in possession of any minimal MBP epitope longer than the sequence consisting of the amino acid sequence of SEQ ID NO: 13 for the claimed fusion protein.

Because the described one species of minimal MBP epitope is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, one of skill in the art would conclude that applicant was not in procession of the claimed genus to show that the applicant would have been in possession of the claimed genus as a whole at the time of filing for the claimed fusion protein. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 17, 21, 70 and 72.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115). Applicant is

directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

7. Claims 69 and 71 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

10. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
September 12, 2008